STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 145769

TO: Lansana Nyalley **Location: 5c21/5c18** **Art Unit: 1621** **Friday, February 25, 2005** **Case Serial Number: 10/751237**	**From: Noble Jarrell** **Location: Biotech-Chem Library** **Rem 1B71** **Phone: 272-2556** **Noble.jarrell@uspto.gov**

Search Notes

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center 145769

Requester's Full Name: LANSANA MYALLEY Examiner #: 80552 Date: 02/23/05

Art Unit: 1621 Phone Number 30_____ Serial Number: 10/751,237

Mail Box and Bldg/Room Location: 5B21/5C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

(A) PROCESS OF DRYING ALENDRONATE TRIHYDRATE COMPRISING: REFLUXING THE COMPOUND WITH ABSOLUTE ETHANOL; PASSING THE MIXTURE THROUGH A BED 3Å MOLECULAR SIEVES; RETURNING THE CONDENSED REFLUX TO THE MIXTURE (b) COOLING THE MIXTURE AND (C) ISOLATING THE COMPOUND;

STRUCTURE: $NH_2CH_2CH_2CH_2C(OH)(P(=O)(OH)O^-Na^+)P(=O)(OH)OH$

~~4-amino-1-hydroxy~~

4-amino-1-hydroxy-1,1-bisphosphonic acid monosodium

****

=> b reg
FILE 'REGISTRY' ENTERED AT 15:27:16 ON 25 FEB 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 23 FEB 2005 HIGHEST RN 836595-43-8
DICTIONARY FILE UPDATES: 23 FEB 2005 HIGHEST RN 836595-43-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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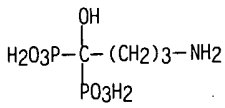
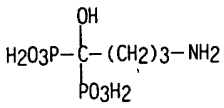
L18 ANSWER 1 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **600116-20-9** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, trihydrate (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 3 H2 O**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
CRN (66376-36-1)



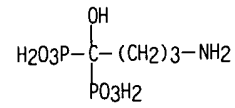
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 2 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **385396-33-8** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, sodium salt, monohydrate (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . H2 O . x Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
CRN (66376-36-1)



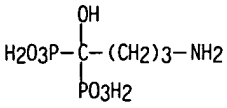
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 3 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **337306-48-6** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monopotassium salt, dihydrate (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 2 H2 O . K**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



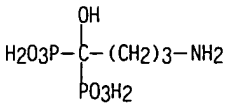
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 4 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **337306-46-4** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monopotassium salt, monohydrate (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . H2 O . K**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
CRN (66376-36-1)



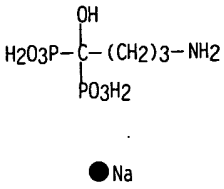
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 5 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-09-2** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, dihydrate (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 2 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



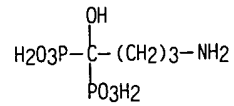
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 6 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-08-1** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (2:3) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 3/2 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



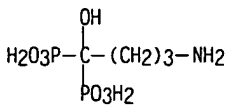
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 7 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-07-0** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (3:4) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 4/3 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



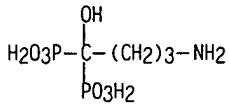
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 8 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-06-9** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (4:5) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 5/4 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



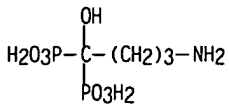
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 9 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-05-8** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Alendronate monosodium monohydrate**
MF **C4 H13 N O7 P2 . H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
CRN (66376-36-1)



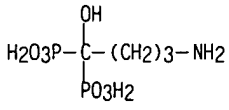
11 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 10 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-04-7** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (4:3) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 3/4 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



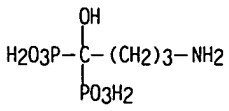
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 11 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-03-6** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (3:2) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 2/3 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



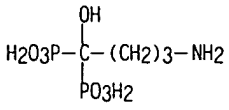
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 12 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-02-5** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (2:1) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 1/2 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



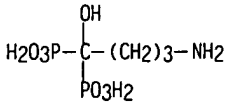
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 13 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-01-4** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (3:1) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 1/3 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



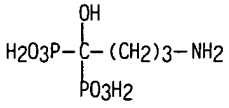
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 14 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **260055-00-3** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (4:1) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 1/4 H2 O . Na**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (66376-36-1)



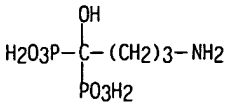
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 15 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **185960-02-5** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, hydrate (2:1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Disodium alendronate hemihydrate**
MF **C4 H13 N O7 P2 . 1/2 H2 O . 2 Na**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
CRN (66376-36-1)



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 16 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **185960-01-4** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, hydrate (2:5) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 5/2 H2 O . 2 Na**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
CRN (66376-36-1)

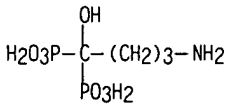


2 Na

5/2 H_2O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 17 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **185960-00-3** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, trihydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Disodium alendronate trihydrate**
MF **C4 H13 N O7 P2 . 3 H2 O . 2 Na**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
CRN (66376-36-1)

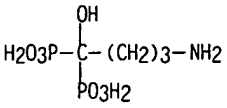


2 Na

3 H_2O

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 18 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **185959-99-3** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, pentahydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Disodium alendronate pentahydrate**
MF **C4 H13 N O7 P2 . 5 H2 O . 2 Na**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
CRN (66376-36-1)

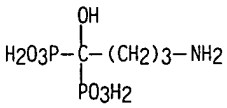


2 Na

5 H_2O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 19 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **185959-98-2** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, monohydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Disodium alendronate monohydrate**
MF **C4 H13 N O7 P2 . H2 O . 2 Na**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
CRN (66376-36-1)

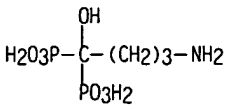


2 Na

H_2O

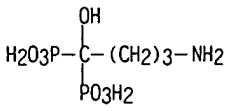
3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 20 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **176513-44-3** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, cadmium salt (1:1), monohydrate (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . Cd . H2 O**
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties)
CRN (66376-36-1)



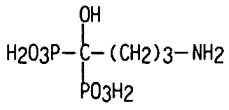
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 21 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **137504-91-7** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (3:4) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 4/3 Ca**
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)
CRN (66376-36-1)



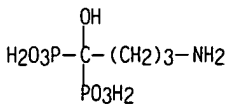
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 22 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **137504-90-6** REGISTRY
CN **Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (2:1) (9CI)** (CA INDEX NAME)
MF **C4 H13 N O7 P2 . 1/2 Ca**
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, IPA, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
CRN (66376-36-1)



3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L18 ANSWER 23 OF 23 REGISTRY COPYRIGHT 2005 ACS on STN
RN **121268-17-5** REGISTRY
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Alendronate monosodium trihydrate**
CN **Alendronate sodium hydrate**
CN Alendronic acid monosodium salt trihydrate
CN Bonalon
CN **Sodium alendronate hydrate**
MF **C4 H13 N O7 P2 . 3 H2 O . Na**
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
CRN (66376-36-1)



66 REFERENCES IN FILE CA (1907 TO DATE)
66 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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(FILE 'HOME' ENTERED AT 15:03:46 ON 25 FEB 2005)

FILE 'HCAPLUS' ENTERED AT 15:04:05 ON 25 FEB 2005
L1 1 (US20040158098 OR US6696601 OR US20030065214 OR US6281381)/PN
E US1999-144461/AP,PRN
L2 1 US1999-144461P/AP,PRN
L3 1 L1-2

FILE 'REGISTRY' ENTERED AT 15:06:06 ON 25 FEB 2005

FILE 'HCAPLUS' ENTERED AT 15:06:08 ON 25 FEB 2005
L4 TRA L3 1- RN : 31 TERMS

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     FILE 'REGISTRY' ENTERED AT 15:06:08 ON 25 FEB 2005
L5          31 SEA L4

     FILE 'WPIX' ENTERED AT 15:06:12 ON 25 FEB 2005
L6           1 (US20040158098 OR US6696601 OR US20030065214 OR US6281381)/PN
               E US1999-144461/AP,PRN
L7           1 US1999-144461P/AP,PRN
L8           1 L6-7

     FILE 'REGISTRY' ENTERED AT 15:12:06 ON 25 FEB 2005
L9         110 C4H13NO7P2
L10          9 L9 AND ALENDRONATE
L11        101 L9 NOT L10
L12         81 L11 AND PHOSPHONIC ACID
L13         44 L12 AND HYDROXYBUTYLIDENE
               SEL RN 3 6-10 14 16-27 29-32 34-41
L14         31 E1-31 AND L13
               SEL RN 13 15 L13
L15          2 E32-33 AND L13
L16         40 L10 OR L14
               SEL RN L16 2 6-16 23-28 33-34 38
L17         21 E34-54 AND L16
L18         23 L15 OR L17

     FILE 'HCAPLUS' ENTERED AT 15:29:18 ON 25 FEB 2005
L19         11 L18 (L) PREP+NT/RL
L20         42 ALENDRONATE (1A) ?SODIUM/BI (1A) ?HYDRATE/BI OR BONALON
L21          2 L20 (L) PREP+NT/RL
L22         11 L19 OR L21
               E FINKELSTEIN N/AU
L23         93 E3-8,E13
               E LIDOR R/AU
L24         21 E3-5
               E LIDOR HADAS/AU
L25         17 E4-5
               E ARONHIME J/AU
L26         53 E3-7
L27        285 (TEVA (1A)PHARM?)/CS,PA
L28          1 L22 AND L23-27
L29         10 L22 NOT L28

     FILE 'WPIX' ENTERED AT 15:38:29 ON 25 FEB 2005
               E ALENDRONIC ACID/CN
               E ALENDRONATE/CN
L30         45 (ALENDRONATE (1A) ?SODIUM (1A) ?HYDRATE OR BONALON)/BIX
               E ALENDRONATE/CN
L31          1 E4
               E ALENDRONATE/DCN
               E ALENDRONIC ACID/DCN
               E ALENDRONIC/DCN
L32         46 L30-31
               E FINKELSTEIN N/AU
L33         19 E3-4
               E LIDOR R/AU
L34          5 E3
               E LIDOR HADAS/AU
L35         19 E4-5
               E ARONHIME J/AU
L36         51 E3
L37        274 (TEVA (1A)PHARM?)/CS,PA
L38          4 L32 AND L33-37
L39         42 L32 NOT L38
L40          2 L39 NOT (PY>1999 OR AY>1999 OR PRY>1999)
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Search done by Noble Jarrell

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=> b hcap
FILE 'HCAPLUS' ENTERED AT 15:48:58 ON 25 FEB 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 25 Feb 2005  VOL 142 ISS 10
FILE LAST UPDATED: 24 Feb 2005  (20050224/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d all fhitstr 128

L28  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2000:161293  HCAPLUS
DN   132:199040
ED   Entered STN:  10 Mar 2000
TI   Sodium alendronate hydrates, processes for their manufacture, and
     pharmaceutical compositions containing them
IN   Finkelstein, Nina; Lidor-Hadas, Ramy; Aronhime,
     Judith
PA   Teva Pharmaceutical Industries Ltd., Israel;
     Teva Pharmaceuticals USA, Inc.
SO   PCT Int. Appl., 56 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   C07F009-38
CC   63-5 (Pharmaceuticals)
     Section cross-reference(s): 1
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2000012517        A1    20000309    WO 1999-US19838        19990827
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
             MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
             SL, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2341459           AA    20000309    CA 1999-2341459        19990827
     AU 9956988           A1    20000321    AU 1999-56988          19990827
     EP 1107974           A1    20010620    EP 1999-944004         19990827
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     US 6281381           B1    20010828    US 1999-384145         19990827
     SI 20581             C     20011231    SI 1999-20070          19990827
     BR 9913472           A     20020305    BR 1999-13472          19990827
     EE 200100126         A     20020617    EE 2001-126            19990827
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	JP 2002523514	T2	20020730	JP 2000-567539	19990827
	NZ 510682	A	20030926	NZ 1999-510682	19990827
	ZA 2001001451	A	20020221	ZA 2001-1451	20010221
	NO 2001000957	A	20010426	NO 2001-957	20010226
	BG 105292	A	20011231	BG 2001-105292	20010226
	LT 4888	B	20020225	LT 2001-16	20010226
	LV 12720	B	20020220	LV 2001-26	20010405
	US 2003065214	A1	20030403	US 2001-898756	20010703
	US 6696601	B2	20040224		
	US 2004158098	A1	20040812	US 2003-751237	20031231
PRAI	US 1998-98313P	P	19980827		
	US 1999-129743P	P	19990416		
	US 1999-144461P	P	19990719		
	US 1999-384145	A1	19990827		
	WO 1999-US19838	W	19990827		
	US 2001-898756	A1	20010703		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000012517	IC	C07F009-38
WO 2000012517	ECLA	C07F009/38A6U
US 6281381	ECLA	C07F009/38A6U
US 2003065214	ECLA	C07F009/38A6U
US 2004158098	ECLA	C07F009/38A6U

AB New hydrate forms of alendronate sodium, having water content of approx. 1-12%, and processes for their manufacture, are disclosed. New crystalline forms of alendronate sodium B, D, E, F, G and H, and processes for manufacturing them, are also disclosed. These new forms of alendronate sodium are suitable for incorporation into pharmaceutical compns. for combating bone resorption in bone diseases.

ST sodium alendronate hydrate prepn pharmaceutical; bone disease sodium alendronate hydrate prepn; resorption bone sodium alendronate hydrate prepn

IT Bone
(demineralization; sodium alendronate hydrates, preparation, and pharmaceutical compns.)

IT Ethers, miscellaneous
RL: MSC (Miscellaneous)
(polyalc.; sodium alendronate hydrates, preparation, and pharmaceutical compns.)

IT Alcohols, miscellaneous
RL: MSC (Miscellaneous)
(polyhydric, and polyalc. ethers; sodium alendronate hydrates, preparation, and pharmaceutical compns.)

IT Drug delivery systems
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)

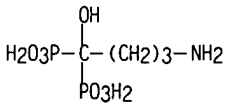
IT Alcohols, miscellaneous
RL: MSC (Miscellaneous)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)

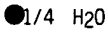
IT 138624-11-0P, Alendronic acid monohydrate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; sodium alendronate hydrates, preparation, and pharmaceutical compns.)

IT 66376-36-1P, Alendronic acid
RL: PNU (Preparation, unclassified); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(reaction; sodium alendronate hydrates, preparation, and pharmaceutical compns.)

IT 124-41-4, Sodium methoxide 141-52-6, Sodium ethoxide 1310-73-2, Sodium hydroxide, reactions 7732-18-5, Water, reactions 121268-17-5 134606-40-9, Disodium alendronate 250665-54-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; sodium alendronate hydrates, preparation, and pharmaceutical

compns.)
IT 129318-43-0P, Monosodium alendronate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT 129318-43-0DP, Monosodium alendronate, hydrates **260055-00-3P**
260055-01-4P 260055-02-5P 260055-03-6P
260055-04-7P 260055-05-8P 260055-06-9P
260055-07-0P 260055-08-1P 260055-09-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT 64-17-5, Ethanol, miscellaneous 67-56-1, Methanol, miscellaneous 67-63-0, 2-Propanol, miscellaneous 67-64-1, Acetone, miscellaneous 67-68-5, DMSO, miscellaneous 68-12-2, DMF, miscellaneous 75-05-8, Acetonitrile, miscellaneous 110-86-1, Pyridine, miscellaneous 123-91-1, Dioxane, miscellaneous 126-33-0, Sulfolane 872-50-4, miscellaneous
RL: MSC (Miscellaneous)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Blum; US 4624947 A 1986 HCAPLUS
(2) Brenner, G; WO 9639149 HCAPLUS
(3) Kieczykowski; US 4922007 A 1990 HCAPLUS
(4) Kieczykowski; US 5019651 A 1991 HCAPLUS
(5) Merck & Co Inc; WO 9639410 A1 1996 HCAPLUS
(6) Stahl; US 4639338 A 1987 HCAPLUS
(7) Stahl; US 4711800 A 1987
IT **260055-00-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
RN 260055-00-3 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, hydrate (4:1) (9CI) (CA INDEX NAME)





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L29 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:895606 HCAPLUS
DN 142:93982

ED Entered STN: 27 Oct 2004
TI Method for preparation of 4-amino-1-hydroxybutyliden-1,1-bisphosphonic acid monosodium trihydrate
IN Kang, Seung An; Lee, Gyeong Hui; Lim, Du Hyeon
PA Yuyu Industrial Co., Ltd., S. Korea
SO Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DT Patent
LA Korean
IC ICM C07F009-38
CC 29-7 (Organometallic and Organometalloidal Compounds)
FAN.CNT 1

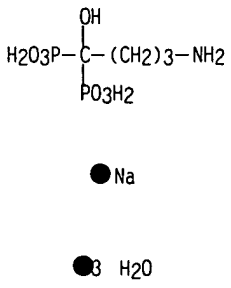
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI KR 2001053355	A	20010625	KR 2001-9980	20010227
PRAI KR 2001-9980		20010227		

CLASS

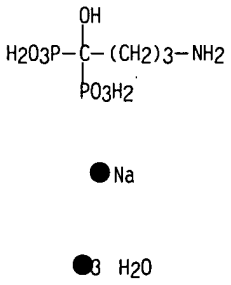
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
KR 2001053355	ICM	C07F009-38

AB Provided is a method for preparation of high purity 4-amino-1-hydroxybutyliden-1,1-bisphosphonic acid monosodium trihydrate safely and cheaply in higher yield. The method for producing 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium trihydrate comprises the steps of: reacting gamma-aminobutylic acid with the mixture of water and triphosphorous chloride; recovering 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid or its salts; dissolving 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid in water with heat and adding sodium hydroxide into the 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid solution in a ratio of 0.9-1:1; and increasing the temperature of the reaction mixture to an appropriate temperature and slowly cooling the mixture

ST aminohydroxybutylidenbisphosphonic acid monosodium trihydrate prepn
IT 56-12-2, .gamma.-Aminobutanoic acid, reactions 7719-12-2, Trichlorophosphine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminohydroxybutylidenbisphonic acid monosodium trihydrate)
IT 66376-36-1P, 4-Amino-1-hydroxybutylidene-1,1-bisphosphonic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminohydroxybutylidenbisphonic acid monosodium trihydrate)
IT **121268-17-5P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of aminohydroxybutylidenbisphonic acid monosodium trihydrate)
IT **121268-17-5P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of aminohydroxybutylidenbisphonic acid monosodium trihydrate)
RN 121268-17-5 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)



L29 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:376014 HCAPLUS
DN 141:207291
ED Entered STN: 10 May 2004
TI A facile and direct synthesis of alendronate from pyrrolidone
AU Xu, Guangyu; Xie, Yuyuan; Wu, Xihan
CS State Key Laboratory of Drug Research Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Shanghai, 201203, Peop. Rep. China
SO Organic Preparations and Procedures International (2004), 36(2), 185-187
CODEN: OPPIAK; ISSN: 0030-4948
PB Organic Preparations and Procedures, Inc.
DT Journal
LA English
CC 29-7 (Organometallic and Organometalloidal Compounds)
OS CASREACT 141:207291
AB A new one-pot procedure to synthesize alendronic acid and corresponding sodium salt from pyrrolidone is reported. Hydrolysis of pyrrolidone in aqueous methanesulfonic acid followed by addition of phosphorus trichloride and pH adjustment using NaOH yielded the monosodium salt in 81% yield.
ST alendronate monosodium salt alendronic acid prepn; pyrrolidone ring opening acid catalyzed reaction phosphorus trichloride
IT 616-45-5, Pyrrolidone 7719-12-2, Phosphorus trichloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(facile and direct synthesis of alendronate from pyrrolidone)
IT 66376-36-1P, Alendronic acid **121268-17-5P**, Alendronic acid monosodium salt trihydrate
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(facile and direct synthesis of alendronate from pyrrolidone)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Gall, R; DE 3623397 1988 HCAPLUS
(2) Kieczykowski, G; US 5039819 1991 HCAPLUS
(3) Kieczykowski, G; J Org Chem 1995, V60, P8310 HCAPLUS
(4) Kubela, R; WO 9834940 1998 HCAPLUS
(5) Liberman, U; N Eng J Med 1995, V333, P1437 HCAPLUS
(6) Llado, J; WO 0110874 2001 HCAPLUS
(7) Widler, L; J Med Chem 2002, V45, P3721 HCAPLUS
IT **121268-17-5P**, Alendronic acid monosodium salt trihydrate
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(facile and direct synthesis of alendronate from pyrrolidone)
RN 121268-17-5 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)



L29 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:868941 HCAPLUS
DN 137:353175

ED Entered STN: 15 Nov 2002
TI Preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid
IN Dabak, Kadir; Zarslan, A. Evren; Sahbaz, Filiz; Aslan, Tuncer
PA EOS Eczacibasi Ozgun Kimyasal Urunler Sanayi Ve Ticaret A.S., Turk.
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
IC C07F009-38
CC 29-7 (Organometallic and Organometalloidal Compounds)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002090367	A1	20021114	WO 2002-TR18	20020508
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	TR 200101250	A2	20030421	TR 2001-200101250	20010510
	CA 2445428	AA	20021114	CA 2002-2445428	20020508
	EP 1390373	A1	20040225	EP 2002-736468	20020508
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004528382	T2	20040916	JP 2002-587445	20020508
	US 2004152916	A1	20040805	US 2003-473600	20031010
PRAI	TR 2001-1250	A	20010510		
	WO 2002-TR18	W	20020508		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002090367	IC	C07F009-38
JP 2004528382	FTERM	4H050/AA02; 4H050/AD17; 4H050/AD30; 4H050/BC10; 4H050/BE04; 4H050/BE10; 4H050/BE50; 4H050/WA12; 4H050/WA15; 4H050/WA26
US 2004152916	ECLA	C07F009/38A6U

OS CASREACT 137:353175
AB The preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid or salts thereof carried out in the presence of ethoxylates or triglycerides is described. Thus, 4-aminobutyric acid is reacted with phosphorous acid and PCl3 in the presence of nonylphenol ethoxylate 4 Mol, followed by hydrolysis with water to give 57% 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt trihydrate.
ST aminohydroxybutylidenebisphosphonic acid prepn manuf ethoxylate triglyceride solvent; phosphonic acid aminohydroxybutylidene prepn manuf ethoxylate triglyceride solvent; alendronate sodium hydrate prepn manuf
IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(ethoxylated; preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and salts thereof by reaction of aminobutyric acid with phosphorous acid and PCl3 in presence of ethoxylates or triglycerides)
IT Glycerides, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and salts thereof by reaction of aminobutyric acid with phosphorous acid and PCl3 in presence of ethoxylates or triglycerides)
IT Corn oil
Olive oil
Sunflower oil

RL: NUU (Other use, unclassified); USES (Uses)
(solvent; preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and salts thereof by reaction of aminobutyric acid with phosphorous acid and PCl3 in presence of ethoxylates or triglycerides)

IT 66376-36-1P, 4-Amino-1-hydroxybutylidene-1,1-bisphosphonic acid
121268-17-5P
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and salts thereof by reaction of aminobutyric acid with phosphorous acid and PCl3 in presence of ethoxylates or triglycerides)

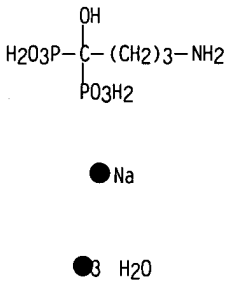
IT 56-12-2, 4-Aminobutyric acid, reactions 7719-12-2, Phosphorous trichloride 13598-36-2, Phosphorous acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and salts thereof by reaction of aminobutyric acid with phosphorous acid and PCl3 in presence of ethoxylates or triglycerides)

IT 3055-96-7, 3,6,9,12,15,18-Hexaoxatriacontan-1-ol 27176-97-2 27177-01-1 27177-08-8
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and salts thereof by reaction of aminobutyric acid with phosphorous acid and PCl3 in presence of ethoxylates or triglycerides)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Apotex Inc; WO 9834940 A 1998 HCAPLUS
(2) Kieczykowski, G; US 4922007 A 1990 HCAPLUS

IT **121268-17-5P**
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and salts thereof by reaction of aminobutyric acid with phosphorous acid and PCl3 in presence of ethoxylates or triglycerides)

RN 121268-17-5 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)



L29 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:249762 HCAPLUS
DN 137:322040
ED Entered STN: 03 Apr 2002
TI Synthesis, characterization and biodistribution of bisphosphonates Sm-153 complexes: correlation with molecular modeling interaction studies
AU Neves, M.; Gano, L.; Pereira, N.; Costa, M. C.; Costa, M. R.; Chandia, M.; Rosado, M.; Fausto, R.
CS Instituto Tecnologico e Nuclear, Sacavem, Port.
SO Nuclear Medicine and Biology (2002), 29(3), 329-338
CODEN: NMBIEO; ISSN: 0969-8051
PB Elsevier Science Inc.

DT Journal
LA English
CC 8-9 (Radiation Biochemistry)
AB Bisphosphonates (BPs) are characterized by a P-C-P backbone structure and two phosphonic acid groups bonded to the same carbon, and are established as osteoclast-mediated bone resorption inhibitors. The nature of the groups attached to the central carbon atom are responsible in determining the potency of bisphosphonates as anti-resorption drugs. However, it is not yet clear the exact relationship between their mol. structure and pharmacol. activities. In this study, mol. geometries of pamidronate, alendronate and neridronate, differing only in the length of the aliphatic chains, were predicted by mol. mechanics and their interactions with hydroxyapatite, the main bone mineral component, were examined We report the synthesis and radiochem. characterization of 153Sm complexes with pamidronate, alendronate and neridronate. Hydroxyapatite binding and biodistribution studies of these complexes have shown a good correlation with the theor. mol. modeling interaction studies. So, it is possible to conclude that computational chemical techniques are a good approach to evaluate specific interactions and may play a relevant role in determining the relative ability of BPs to mineral bone, and open new perspectives to the design of new BPs with increased pharmacol. activity. These techniques could be extended to BPs as ligands to carrier radioactive metals, aiming for new bone therapeutic radiopharmaceuticals.
ST samarium 153 bisphosphonate prepn mol modeling hydroxyapetite binding; bone resorption inhibitor samarium 153 bisphosphonate complex biodistribution
IT Bone
(resorption, inhibitors; synthesis, characterization and biodistribution of bisphosphonates Sm-153 complexes: correlation with mol. modeling of hydroxyapetite bone mineral interaction studies)
IT Molecular modeling
(synthesis, characterization and biodistribution of bisphosphonates Sm-153 complexes: correlation with mol. modeling of hydroxyapetite bone mineral interaction studies)
IT 1306-06-5, Hydroxyapatite
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis, characterization and biodistribution of bisphosphonates Sm-153 complexes: correlation with mol. modeling of hydroxyapetite bone mineral interaction studies)
IT 15766-00-4DP, Samarium 153, complexes with biphosphonates, biological studies 40391-99-9DP, samarium 153 complexes 66376-36-1DP, Alendronate, samarium 153 complexes 79778-41-9DP, Neridronate, samarium 153 complexes
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, characterization and biodistribution of bisphosphonates Sm-153 complexes: correlation with mol. modeling of hydroxyapetite bone mineral interaction studies)
IT **121268-17-5P, Alendronate monosodium trihydrate** 473435-32-4P 473435-34-6P
RL: PRP (Properties); **SPN (Synthetic preparation); PREP (Preparation)**
(synthesis, characterization and biodistribution of bisphosphonates Sm-153 complexes: correlation with mol. modeling of hydroxyapetite bone mineral interaction studies)
IT 56-12-2, reactions 60-32-2 107-95-9, .beta.-Alanine
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis, characterization and biodistribution of bisphosphonates Sm-153 complexes: correlation with mol. modeling of hydroxyapetite bone mineral interaction studies)
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Barnett, B; Acta Cryst 1979, VB35, P1212 HCAPLUS

(2) Black, N; J Chem Soc Faraday Trans 1991, V87, P3409
(3) Boissier, S; Cancer Res 2000, V60, P2949 HCAPLUS
(4) Burket, U; ACS Monograph 1982, V177
(5) Coveney, P; J Chem Soc Faraday Trans 1996, V92, P831 HCAPLUS
(6) Deutsch, E; Prog Inorg Chem 1983, V30, P75 HCAPLUS
(7) Fleisch, H; Endocrine Rev 1998, V19, P80 HCAPLUS
(8) Fleisch, H; Science 1969, V165, P1264
(9) Francis, M; J Nucl Med 1980, V21, P1189
(10) Fromigue, O; J Bone Min Res 2000, V15, P2211 HCAPLUS
(11) Green, J; Breast Cancer Res 2000, V3(Suppl 1), PA28
(12) Huigen, Y; Appl Radiat Isot 1990, V41, P189 HCAPLUS
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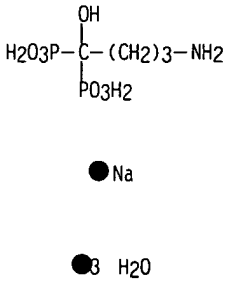
(14) Jurisson, S; Inorg Chem 1983, V22, P1332 HCAPLUS
(15) Kay, M; Nature 1964, V204, P1050 HCAPLUS
(16) Ketring, A; Nucl Med Biol 1987, V14, P223 HCAPLUS
(17) Kieczyowski, G; J Org Chem 1995, V60, P8310
(18) Liberman, U; N Engl J Med 1995, V333, P1437 HCAPLUS
(19) Libson, K; J Am Chem Soc 1980, V102, P2476 HCAPLUS
(20) Masarachia, P; Bone 1996, V19, P281 HCAPLUS
(21) McEwan, A; Semin Radiat Oncol 2000, V10, P103 MEDLINE
(22) Mohamed, A; J Chromat 1989, V488, P463
(23) Molecular Simulations Inc; Cerius-2 (Version 3.5) 1997
(24) Mundy, G; Semin Oncol 2001, V28, P35 MEDLINE
(25) Nash, K; Inorg Chem 1995, V34, P2753 HCAPLUS
(26) Nash, K; Inorg Chim Acta 1998, V269, P211 HCAPLUS
(27) Niketic, S; lecture notes in chemistry 1985, V3
(28) Rogers, M; Bone 1999, V24, P73S HCAPLUS
(29) Russell, R; Bone 1999, V25, P97 HCAPLUS
(30) Saag, K; N Engl J Med 1998, V339, P292 HCAPLUS
(31) Shakespeare, W; Proc Natl Acad Sci 2000, V97, P9373 HCAPLUS
(32) Vega, D; Acta Cryst 1996, VC52, P2198 HCAPLUS
(33) Zeevaart, J; J Inorg Biochem 1999, V73, P265 HCAPLUS

IT **121268-17-5P, Alendronate monosodium trihydrate**
RL: PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**
(synthesis, characterization and biodistribution of bisphosphonates Sm-153 complexes: correlation with mol. modeling of hydroxyapetite bone mineral interaction studies)

RN 121268-17-5 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monosodium salt, trihydrate (9CI) (CA INDEX NAME)



L29 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:319901 HCAPLUS
DN 134:326626
ED Entered STN: 04 May 2001
TI Novel salts of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid, their preparation and use

IN Treppendahl, Svend Peter; Petersen, Hanne Borgelin; Jensen, Lotte Basse; Pedersen, Soren Bols
PA A/S Gea Farmaceutisk Fabrik, Den.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07F009-38
ICS A61K031-663; A61P019-08; A61P013-04
CC 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001030788	A1	20010503	WO 2000-DK589	20001024
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 20020942	U1	20020829	DE 2000-20022942	20001024
PRAI	DK 1999-1536	A	19991026		
	WO 2000-DK589	W	20001024		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001030788	ICM	C07F009-38
	ICS	A61K031-663; A61P019-08; A61P013-04
DE 20020942	ECLA	C07F009/38A6U

AB The monopotassium salt of 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and hydrates thereof, particularly the monohydrate and the dihydrate, pharmaceutical prepns. containing such salts as active ingredient, a method for preparing them and their use for treatment or prophylaxis of diseases relating to the calcium metabolism are described.

ST amino hydroxybutylidene bisphosphonate salt prepn pharmaceutical compn; alendronic acid salt prepn pharmaceutical compn

IT Drugs
(preparation, pharmaceutical composition, and use of novel salts of aminohydroxybutylidene bisphosphonic acid)

IT 165043-20-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, pharmaceutical composition, and use of novel salts of aminohydroxybutylidene bisphosphonic acid)

IT **337306-46-4P** 337306-47-5P
RL: RCT (Reactant); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation, pharmaceutical composition, and use of novel salts of aminohydroxybutylidene bisphosphonic acid)

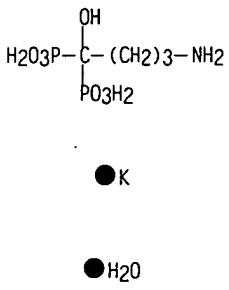
IT **337306-48-6P**
RL: **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation, pharmaceutical composition, and use of novel salts of aminohydroxybutylidene bisphosphonic acid)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

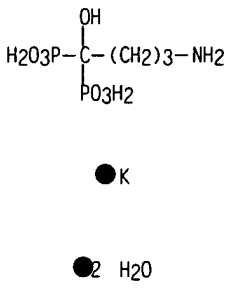
RE

(1) Gerard, R; US 4922007 A 1990 HCAPLUS
(2) Merck & Co; WO 9639149 A 1996 HCAPLUS
(3) Merck & Co; WO 9639410 A 1996 HCAPLUS

(4) Unipharm Ltd: WO 9920635 A 1999 HCAPLUS
IT **337306-46-4P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation, pharmaceutical composition, and use of novel salts of aminohydroxybutylidene bisphosphonic acid)
RN 337306-46-4 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monopotassium salt, monohydrate (9CI) (CA INDEX NAME)



IT **337306-48-6P**
RL: **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation, pharmaceutical composition, and use of novel salts of aminohydroxybutylidene bisphosphonic acid)
RN 337306-48-6 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, monopotassium salt, dihydrate (9CI) (CA INDEX NAME)



L29 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:105205 HCAPLUS
DN 126:122508
ED Entered STN: 14 Feb 1997
TI Bisphosphonate cement composition to prevent aseptic loosening of orthopedic implant devices
IN Simpson, Hamish; Athanasou, Nick; Yates, Ashley J.
PA Merck and Co., Inc., USA; Simpson, Hamish; Athanasou, Nick; Yates, Ashley J.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61F002-28
ICS A61K006-08

CC 63-7 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9639107	A1	19961212	WO 1996-US8515	19960603
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN				
	RW: KE, LA, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2223450	AA	19961212	CA 1996-2223450	19960603
	EP 831756	A1	19980401	EP 1996-917041	19960603
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 11511041	T2	19990928	JP 1996-501089	19960603
PRAI	US 1995-470404	A	19960603		
	WO 1996-US8515	W	19960603		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9639107	ICM	A61F002-28
	ICS	A61K006-08
WO 9639107	ECLA	A61K031/66H15; A61L024/00H2; A61L024/04P+C08L33/06; A61L024/04P+C08L33/12; C07F009/38A6U

AB Disclosed is a bisphosphonate bone cement for preventing peri-prosthetic bone loss and aseptic loosening of a joint prosthesis in patients, which cement contains a bisphosphonate bone resorption inhibitor, e.g. Na or Ca salt of alendronate and a pharmaceutically acceptable polymeric carrier such as poly(Me methacrylate). A composition containing Me methacrylate, N,N-dimethyl-p-toluidine, and chlorophyll was added to a composition containing Me methacrylate-Me acrylate copolymer, benzoyl peroxide, ZrO2, chlorophyll, and gentamicin, then alendronate Na was added to give a cement mixture

ST bone cement bisphosphonate polymethacrylate

IT Medical goods
(bone cements; bone implant cements containing bisphosphonate bone resorption inhibitor and polymeric carrier)

IT Bone
(resorption, inhibitors; bone implant cements containing bisphosphonate bone resorption inhibitor and polymeric carrier)

IT **185959-98-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(bone implant cements containing bisphosphonate bone resorption inhibitor and polymeric carrier)

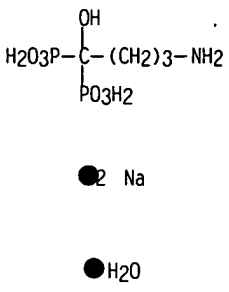
IT 9003-42-3, Polyethyl methacrylate 9011-14-7, Polymethyl methacrylate 9011-87-4, Methyl methacrylatemethyl acrylate copolymer 10596-23-3 40391-99-9 75755-07-6, Piridronic acid 89987-06-4, Tiludronic acid 94232-19-6 105462-24-6 114084-78-5, Ibandronic acid 129318-43-0, Alendronate sodium 137504-89-3 138330-18-4, YM 175 138366-79-7 157432-53-6 186090-69-7 186090-70-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone implant cements containing bisphosphonate bone resorption inhibitor and polymeric carrier)

IT **185959-98-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(bone implant cements containing bisphosphonate bone resorption inhibitor and polymeric carrier)

RN 185959-98-2 HCAPLUS

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt,

monohydrate (9CI) (CA INDEX NAME)



L29 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:94095 HCAPLUS
DN 126:108945
ED Entered STN: 10 Feb 1997
TI Disodium alendronate formulations
IN Brenner, Gerald S.; Oberholtzer, Earl R., Jr.; Thies, J. Eric
PA Merck and Co., Inc., USA
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07F009-38
ICS A61K031-66
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9639410	A1	19961212	WO 1996-US8399	19960603
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2221844	AA	19961212	CA 1996-2221844	19960603
	AU 9661483	A1	19961224	AU 1996-61483	19960603
	EP 837863	A1	19980429	EP 1996-919036	19960603
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 11506757	T2	19990615	JP 1997-501011	19960603
	US 2001021705	A1	20010913	US 2001-841126	20010424
PRAI	US 1995-469142	A1	19950606		
	WO 1996-US8399	W	19960603		
	US 1997-973384	A1	19971203		
	US 2000-476274	A1	20000103		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9639410	ICM	C07F009-38
	ICS	A61K031-66
US 2001021705	ECLA	A61K031/66H15; C07F009/38A6U

AB A method for treating and preventing bone loss in patients by administering a formulation of disodium alendronate, or its hydrates and formulations is described. Thus, alendronic acid was treated with 0.5N NaOH to give disodium salt monohydrate. The solubility of this salt was 200 mg/mL.

ST disodium alendronate hydrate formulation prepn; bone loss disodium alendronate hydrate

IT Bone
(demineralization; disodium alendronate formulations)

IT Osteoporosis
(disodium alendronate formulations)

IT 66376-36-1, Alendronic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(disodium alendronate formulations)

IT **185959-98-2P, Disodium Alendronate monohydrate 185959-99-3P, Disodium Alendronate pentahydrate 185960-00-3P, Disodium Alendronate trihydrate 185960-01-4P 185960-02-5P, Disodium Alendronate hemihydrate**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(**disodium alendronate** formulations)

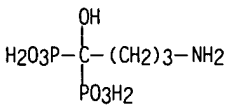
IT 134606-40-9P, Disodium Alendronate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(disodium alendronate formulations)

IT 138624-11-0, Alendronic acid monohydrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disodium alendronate formulations)

IT **185959-98-2P, Disodium Alendronate monohydrate 185959-99-3P, Disodium Alendronate pentahydrate 185960-00-3P, Disodium Alendronate trihydrate 185960-01-4P 185960-02-5P, Disodium Alendronate hemihydrate**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(**disodium alendronate** formulations)

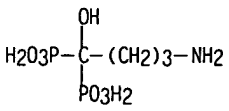
RN 185959-98-2 HCAPLUS

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, monohydrate (9CI) (CA INDEX NAME)



RN 185959-99-3 HCAPLUS

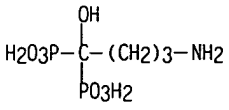
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, pentahydrate (9CI) (CA INDEX NAME)



●2 Na

●5 H_2O

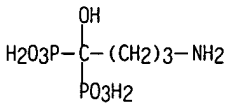
RN 185960-00-3 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, trihydrate (9CI) (CA INDEX NAME)



●2 Na

●3 H_2O

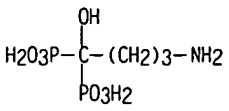
RN 185960-01-4 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, hydrate (2:5) (9CI) (CA INDEX NAME)



●2 Na

●5/2 H_2O

RN 185960-02-5 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, disodium salt, hydrate (2:1) (9CI) (CA INDEX NAME)

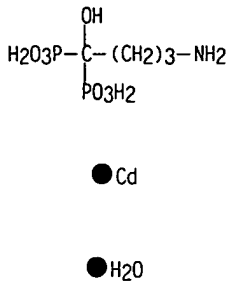


2 Na

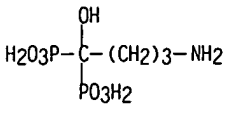
1/2 H_2O

L29 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:204781 HCAPLUS
DN 124:330704
ED Entered STN: 10 Apr 1996
TI Complexation of cadmium and zinc with alendronate (4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid)
AU Dufau, C.; Benramdane, M.; Leroux, Y.; El Manouni, D.; Neuman, A.; Prange, T.; Silvestre, J.-P.; Gillier, H.
CS Chimie Structurale Biomoleculaire, UFR, Bobigny, 93012, Fr.
SO Phosphorus, Sulfur and Silicon and the Related Elements (1995), 107(1-4), 145-59
CODEN: PSSLEC; ISSN: 1042-6507
PB Gordon & Breach
DT Journal
LA French
CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 75
AB The title cadmium and zinc alendronate complexes Zn[NH3+(CH2)3C(OH)(PO3H-)2]2.2H2O (I) and Cd[NH3+(CH2)3C(OH)(PO3H-)(PO32-)].H2O (II) were prepared from alendronate and ZnSO4 or CdCO3, resp. The structures of the complexes were determined by x-ray crystallog. (complex I, monoclinic, space group P21/c; complex II, monoclinic, space group P21/n). The study points out that the size of the cation strongly modifies the structure of the complex. With Cu(II) and Zn(II), which are cations with similar ionic radii, one cation is put in the center of the coordination system, and the structures are isomorphous. However, with Cd(II), a binuclear complex was obtained. Results are discussed on the basis of these structures..
ST crystal structure calcium zinc alendronate; supramol structure calcium zinc alendronate; calcium alendronate prepn structure; zinc alendronate prepn structure; alendronate calcium zinc prepn structure; aminohydroxybutylidenebisphosphonate calcium zinc prepn structure
IT Crystal structure
Molecular structure
(of calcium and zinc alendronates)
IT 66376-36-1, Alendronate
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of calcium and zinc alendronates)
IT 7733-02-0, Zinc sulfate (ZnSO4)
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of zinc alendronate)
IT 176513-43-2P **176513-44-3P**
RL: PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation and crystal structure of)
IT **176513-44-3P**
RL: PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation and crystal structure of)
RN 176513-44-3 HCAPLUS

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, cadmium salt (1:1), monohydrate (9CI) (CA INDEX NAME)



L29 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:502740 HCAPLUS
DN 122:298947
ED Entered STN: 21 Apr 1995
TI Development of subcutaneous and intramuscular formulations of calcium alendronate salts
AU Ostovic, Drazen; Brenner, Gerald S.
CS Dep. Pharm. Res. Development, Merck Res. Lab., West Point, PA, 19486, USA
SO Drug Development and Industrial Pharmacy (1995), 21(10), 1157-69
CODEN: DDIPD8; ISSN: 0363-9045
PB Dekker
DT Journal
LA English
CC 63-6 (Pharmaceuticals)
AB Poorly soluble calcium alendronate salts were prepared and investigated as potential candidates for s.c. or i.m. formulations. Three such formulations containing calcium alendronate salts with different stoichiometries were developed for testing in safety, disposition and efficacy studies in animals. All formulations demonstrated a drastic reduction in pain on injection and tissue damaging propensity compared to the soluble salts of alendronate. All three were efficacious and showed prolonged absorption from the injection site with the deposition of a large percentage of the dose into the bone. Complex formation between alendronate and calcium was also studied.
ST calcium alendronate subcutaneous intramuscular injection
IT Pharmaceutical dosage forms
(injections, i.m., s.c. and i.m. formulations of calcium alendronate)
IT Pharmaceutical dosage forms
(injections, s.c., s.c. and i.m. formulations of calcium alendronate)
IT **137504-90-6P**
RL: **PNU (Preparation, unclassified)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(s.c. and i.m. formulations of calcium alendronate)
IT 10043-52-4, Calcium chloride, reactions 129318-43-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(s.c. and i.m. formulations of calcium alendronate)
IT **137504-90-6P**
RL: **PNU (Preparation, unclassified)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(s.c. and i.m. formulations of calcium alendronate)
RN 137504-90-6 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (2:1) (9CI) (CA INDEX NAME)



●1/2 Ca

L29 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:670695 HCAPLUS
DN 115:270695
ED Entered STN: 27 Dec 1991
TI Use of bisphosphonic acid calcium salts for the treatment of calcium metabolism disorders
IN Brenner, Gerald S.; Ostovic, Drazen
PA Merck and Co., Inc., USA
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K031-66
CC 1-10 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

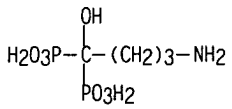
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 449405	A2	19911002	EP 1991-300740	19910130
	EP 449405	A3	19921021		
	EP 449405	B1	19980812		
	R: CH, DE, FR, GB, IT, LI, NL				
	CA 2035179	AA	19910801	CA 1991-2035179	19910129
	CA 2035179	C	20010814		
	JP 04211015	A2	19920803	JP 1991-10556	19910131
	JP 3033783	B2	20000417		
	US 5356887	A	19941018	US 1993-118832	19930907
PRAI	US 1990-472987	A	19900131		
	US 1990-561026	A	19900801		
	US 1991-714467	B1	19910613		
	US 1992-924432	B1	19920731		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 449405	ICM	A61K031-66
EP 449405	ECLA	A61K031/66

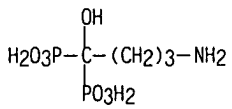
AB An insol. bisphosphonic acid Ca salt, e.g. di[4-amino-1-hydroxybutylidene)-1,1-bisphosphonic acid] monocalcium salt (I), is formulated into an aqueous suspension for i.m. and s.c. administration in the prevention or treatment of Ca metabolism disturbances. The Ca salts provide a slow systemic release of the bisphosphonic acid and reduce tissue damage and localized pain and irritation. Thus, I was suspended in a vehicle containing Na CMC, NaCl, NaOc, and distilled water. S.c. administration of the suspension of I to rats exhibited a lower tendency to induce irritation at the site of injection, compared to the solution of [(4-amino-1-hydroxybutylidene)-1,1-bisphosphonic acid] Na salt (II), and the bone loss in rats undergoing immobilization surgery was less than the control group treated with II.
ST calcium metab disorder bisphosphonate suspension; bone loss calcium aminohydroxybutylidene bisphosphonate
IT Osteoporosis
(treatment of, (aminohydroxybutylidene)bisphosphonic acid calcium salts for)

IT Bone, disease or disorder
(demineralization, treatment of, (aminohydroxybutylidene)bisphosphonic acid calcium salts for)
IT Pharmaceutical dosage forms
(injections, emulsions, of (aminohydroxybutylidene)bisphosphonic acid calcium salts, for treatment of calcium metabolic disorders)
IT 66376-36-1
RL: PROC (Process)
(conversion of, to sodium salt)
IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(metabolic disorders, treatment of, (aminohydroxybutylidene)bisphosphonic acid calcium salts for)
IT 129318-43-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to calcium salt)
IT 137504-89-3P **137504-90-6P 137504-91-7P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, for treatment of calcium metabolic disorders)
IT **137504-90-6P 137504-91-7P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, for treatment of calcium metabolic disorders)
RN 137504-90-6 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (2:1) (9CI) (CA INDEX NAME)



●1/2 Ca

RN 137504-91-7 HCAPLUS
CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis-, calcium salt (3:4) (9CI) (CA INDEX NAME)



●4/3 Ca

=> b wpix
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FOR DETAILS. <<<

=> d all l38 tot

L38 ANSWER 1 OF 4 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2003-618086 [58] WPIX
CR 2003-845092 [78]
DNC C2003-168622
TI Solid pharmaceutical dosage form useful for oral delivery of drug e.g. non-steroidal antiinflammatory drug comprises core tablet containing an active ingredient sheathed in annular body of compressed powder or granular material.
DC B05 B07
IN AQUA, O; FLESHNER-BARAK, M; LERNER, E I; ROSENBERGER, V; FLASHNER-BARAK, M; LERNER, I E; ROSEMBERGER, V
PA (TEVA-N) **TEVA PHARM IND LTD**; (AQUA-I) AQUA O; (FLES-I) FLESHNER-BARAK M; (LERN-I) LERNER E I; (ROSE-I) ROSENBERGER V; (FLAS-I) FLASHNER-BARAK M; (TEVA-N) **TEVA PHARM USA INC**
CYC 103
PI WO 2003057136 A2 20030717 (200358)* EN 41 A61K000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
US 2003206954 A1 20031106 (200374) A61K031-66
AU 2002352613 A1 20030724 (200421) A61K000-00
US 2004052843 A1 20040318 (200421) A61K031-716
EP 1465606 A2 20041013 (200467) EN A61K009-24
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
KR 2004073512 A 20040819 (200501) A61K009-24
EP 1492508 A1 20050105 (200504) EN A61K009-20
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
BR 2002015413 A 20041214 (200510) A61K009-24
ADT WO 2003057136 A2 WO 2002-US36081 20021112; US 2003206954 A1 Provisional US 2001-342442P 20011224, Provisional US 2002-361821P 20020304, Cont of US 2002-291619 20021112, US 2003-419536 20030421; AU 2002352613 A1 AU 2002-352613 20021112; US 2004052843 A1 Provisional US 2001-342442P 20011224, Provisional US 2002-361821P 20020304, CIP of US 2002-291619

20021112, US 2003-379338 20030303; EP 1465606 A2 EP 2002-789567 20021112, WO 2002-US36081 20021112; KR 2004073512 A KR 2004-710037 20040624; EP 1492508 A1 EP 2003-713882 20030303, WO 2003-US6591 20030303; BR 2002015413 A BR 2002-15413 20021112, WO 2002-US63081 20021112

FDT AU 2002352613 A1 Based on WO 2003057136; EP 1465606 A2 Based on WO 2003057136; EP 1492508 A1 Based on WO 2003075893; BR 2002015413 A Based on WO 2003057136

PRAI US 2002-361821P 20020304; US 2001-342442P 20011224; US 2002-291619 20021112; US 2003-419536 20030421; US 2003-379338 20030303

IC ICM A61K000-00; A61K009-20; A61K009-24; A61K031-66; A61K031-716
ICS A61K009-22; A61K009-28; A61K009-30; A61K009-44; A61K031-192; A61K031-198; A61K031-24; A61K031-405; A61K031-60; B29C043-20; B30B011-08

AB WO2003057136 A UPAB: 20050211
NOVELTY - A solid pharmaceutical dosage form (I) comprises a core tablet containing an active pharmaceutical ingredient sheathed in an annular body of compressed powder or granular material formed by compression around the core tablet.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a toolset (II) for producing (I) comprising a columnar punch and a punch assembly comprising annular punch and a core rod slidably engageable with the annulus of the annular punch. The core rod is capable of movement between a retracted position and an extended position. The core rod is biased in an extended position; and

(2) production of solid dosage form involving forming annular body of powder or granular material around core tablet by compression.

ACTIVITY - Antiulcer; Antiinflammatory.

MECHANISM OF ACTION - None given.

USE - For oral delivery of drug e.g. non-steroidal antiinflammatory drugs (claimed) that causes irritation or ulceration to the lining of esophagus and stomach.

ADVANTAGE - The solid dosage form releases drug to a predetermined release profile and reduces contact of the drug to the mucosa lining of the gastrointestinal tract.

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-C02A; B04-C02A1; B04-C02A2; B04-C02B2; B04-C03A; B05-B01G; B05-B01P; B06-D01; B06-D04; B06-E05; B06-F02; B06-F03; B07-A02A; B07-A02B; B07-D02; B07-D08; B07-E01; B10-A10; B10-B02A; B10-C03; B10-C04B; B10-C04C; B12-M02E; B12-M10; B12-M11B; B12-M11D; B12-M11G; B14-C03

L38 ANSWER 2 OF 4 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-289762 [28] WPIX

CR 2004-533992 [51]

DNC C2003-075148

TI Oral pharmaceutical dosage form, useful for treating bone diseases, provides immediate release of a vitamin D derivative and delayed release of a therapeutic bisphosphonate.

DC A96 B05

IN FLESHNER-BARAK, M

PA (TEVA-N) **TEVA PHARM IND LTD**; (FLES-I) FLESHNER-BARAK M; (TEVA-N) **TEVA PHARM USA INC**

CYC 101

PI WO 2003007916 A1 20030130 (200328)* EN 24 A61K009-20
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM

ZW
US 2003158154 A1 20030821 (200356) A61K031-675
EP 1416919 A1 20040512 (200431) EN A61K009-20
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
AU 2002320605 A1 20030303 (200452) A61K009-20
ADT WO 2003007916 A1 WO 2002-US22825 20020717; US 2003158154 A1 Provisional US 2001-305913P 20010717, US 2002-196766 20020717; EP 1416919 A1 EP 2002-750134 20020717, WO 2002-US22825 20020717; AU 2002320605 A1 AU 2002-320605 20020717
FDT EP 1416919 A1 Based on WO 2003007916; AU 2002320605 A1 Based on WO 2003007916
PRAI US 2001-305913P 20010717; US 2002-196766 20020717
IC ICM A61K009-20; A61K031-675
ICS A61K009-22; A61K009-48; A61K031-59; A61K031-66
AB WO2003007916 A UPAB: 20050217
NOVELTY - Oral pharmaceutical dosage form provides immediate or uncontrolled release of a vitamin D derivative (I) and delayed release of a therapeutic bisphosphonate (II) at least an hour after the release of (I).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) Combination therapy for treating a bone disease, comprising repeated administration of a unit dosage form that releases a calcium transport stimulator in an immediate or uncontrolled manner and, after swelling to a size that prevents passage through the pylorus and after a delay allowing the calcium transport stimulator to deplete the upper gastrointestinal tract of calcium, releases a therapeutic bisphosphonate in the stomach; and

(2) Combination therapy for treating a bone disease, comprising administering a unit pre-dose of a vitamin D derivative and, 2-6 hours later, administering a therapeutic bisphosphonate.

ACTIVITY - Osteopathic; Cytostatic.

No biological data available.

MECHANISM OF ACTION - None given.

USE - The dosage form is used for treating bone diseases, especially metastatic bone disease, osteoporosis, Paget's disease, hypercalcemia and bone cancer (all claimed) or for inhibiting bone resorption (claimed).

ADVANTAGE - (I) stimulates the transport of calcium from the intestine into the bloodstream, providing a low-calcium environment that will enhance absorption of (II) when it is released.

Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A12-V01; B03-G; B12-M10B; B12-M11B; B14-H01; B14-N01

L38 ANSWER 3 OF 4 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2002-205919 [26] WPIX
CR 2002-241287 [29]; 2003-092803 [08]; 2003-155983 [15]
DNC C2002-063074
TI Use of non-hydrated hydrogel in pharmaceutical oral dosage form for treating bone disease.
DC A11 A96 B05 B07
IN DAHAN, M; FLASHNER-BARAK, M; LERNER, Y; ROSENBERGER, V
PA (TEVA-N) **TEVA PHARM IND LTD**; (DAHA-I) DAHAN M; (FLAS-I) FLASHNER-BARAK M; (LERN-I) LERNER Y; (ROSE-I) ROSENBERGER V; (TEVA-N) **TEVA PHARM USA INC**
CYC 97
PI WO 2002000204 A1 20020103 (200226)* EN 28 A61K009-22
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
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US 2002015733 A1 20020207 (200226) A61K031-66
AU 2001068719 A 20020108 (200235) A61K009-22
US 6476006 B2 20021105 (200276) A01N057-26
EP 1296657 A1 20030402 (200325) EN A61K009-22
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
KR 2003013460 A 20030214 (200339) A61K031-24
KR 2003023879 A 20030320 (200346) A61K009-22
HU 2003001400 A2 20030929 (200369) A61K009-22
US 2003203878 A1 20031030 (200372) A61K031-685
JP 2004501186 W 20040115 (200410) 48 A61K031-663
CZ 2003000211 A3 20040317 (200430) A61K009-22

ADT WO 2002000204 A1 WO 2001-US20130 20010622; US 2002015733 A1 Provisional US 2000-213832P 20000623, Provisional US 2001-260438P 20010109, US 2001-770898 20010126; AU 2001068719 A AU 2001-68719 20010622; US 6476006 B2 Provisional US 2000-213832P 20000623, Provisional US 2001-260438P 20010109, US 2001-770898 20010126; EP 1296657 A1 EP 2001-946706 20010622, WO 2001-US20130 20010622; KR 2003013460 A KR 2002-717538 20021223; KR 2003023879 A KR 2002-717536 20021223; HU 2003001400 A2 WO 2001-US20130 20010622, HU 2003-1400 20010622; US 2003203878 A1 Provisional US 2000-213832P 20000623, Provisional US 2001-260438P 20010109, Cont of US 2001-770898 20010126, Cont of US 2002-246502 20020916, US 2003-420403 20030422; JP 2004501186 W WO 2001-US20130 20010622, JP 2002-504986 20010622; CZ 2003000211 A3 WO 2001-US20130 20010622, CZ 2003-211 20010622

FDT AU 2001068719 A Based on WO 2002000204; EP 1296657 A1 Based on WO 2002000204; HU 2003001400 A2 Based on WO 2002000204; US 2003203878 A1 Cont of US 6476006; JP 2004501186 W Based on WO 2002000204; CZ 2003000211 A3 Based on WO 2002000204

PRAI US 2001-770898 20010126; US 2000-213832P 20000623;
US 2001-260438P 20010109; US 2000-217110P 20000710;
US 2000-223212P 20000804; US 2002-246502 20020916;
US 2003-420403 20030422

IC ICM A01N057-26; A61K009-22; A61K031-24; A61K031-66; A61K031-663; A61K031-685
ICS A61K009-14; A61K009-34; A61K009-36; A61K031-675; A61K031-7024; A61K047-04; A61K047-26; A61K047-32; A61K047-36; A61K047-38; A61P003-14; A61P019-00; A61P019-08; A61P019-10

AB WO 200200204 A UPAB: 20040511

NOVELTY - A pharmaceutical dosage form for oral administration comprises a bis-phosphonate and a drug delivery vehicle which contains a non-hydrated hydrogel.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a coated pharmaceutical dosage form comprising a core containing the bis-phosphonate and optionally other excipient and a coating around the core containing the hydrogel, the superdisintegrant and tannic acid; and

(2) making of the dosage form involving mixing powdered **sodium alendronate monohydrate**, microcrystalline cellulose and lactose, tableting the mixed powders to make core, dry mixing the hydroxypropyl methylcellulose (HPMC), tannic acid, hydroxypropyl cellulose (HPC), and cross-linked carboxymethyl sodium to produce a coating mix, embedding the core in the coating mix, and compacting the coating mix.

ACTIVITY - Osteopathic; cytostatic.

MECHANISM OF ACTION - Inhibitor.

USE - For treating bone disease, e.g. metastatic bone disease, Paget's disease or osteoporosis, hypercalcemia, malignancy in bone and inhibiting bone resorption (claimed).

ADVANTAGE - The dosage form when contacted with gastric fluid or stimulated gastric fluid, hydrates the non-hydrated hydrogel and expands the delivery vehicle, thus provides delayed gastric release of the bis-phosphonate for at least 2 (preferably at least 3, especially at least 4) hours. The dosage form swells rapidly by a factor of at least 5

(preferably at least 8) within 15 minutes (preferably within 5) minutes of contacting aqueous solution. The dosage is administered in a controlled manner. The oral dosage form swells rapidly in the gastric juices of the patient, thus increasing the likelihood of the dosage to be released in the stomach or duodenum.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-C02A; B04-C02A2; B04-C03A; B05-A01B; B05-B01P; B10-E02; B12-M11; B14-H01B; B14-L06; B14-N01

L38 ANSWER 4 OF 4 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2000-246722 [21] WPIX
DNC C2000-074753
TI New 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt with specified water content used to treat and/or prevent bone loss.
DC B05
IN **ARONHIME, J**; **FINKELSTEIN, N**; **LIDOR-HADAS, R**; **LIDOR-HAMAS, R**
PA (TEVA-N) **TEVA PHARM IND LTD**; (TEVA-N) **TEVA PHARM USA INC** ; (ARON-I) ARONHIME J; (FINK-I) FINKELSTEIN N; (LIDO-I) LIDOR-HADAS R
CYC 89
PI WO 2000012517 A1 20000309 (200021)* EN 56 C07F009-38
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
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AU 9956988 A 20000321 (200031)
NO 2001000957 A 20010426 (200131) C07F009-38
EP 1107974 A1 20010620 (200135) EN C07F009-38
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KR 2001079701 A 20010822 (200213) C07F009-38
SK 2001000248 A3 20020107 (200213) C07F009-38
BR 9913472 A 20020305 (200225) C07F009-38
ZA 2001001451 A 20020424 (200237) 65 C07F000-00
MX 2001002017 A1 20010801 (200238) C07F009-38
JP 2002523514 W 20020730 (200264) 64 C07F009-38
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NZ 510682 A 20030926 (200366) C07F009-38
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AU 2004202301 A1 20040624 (200468)# C07F009-38
ADT WO 2000012517 A1 WO 1999-US19838 19990827; AU 9956988 A AU 1999-56988 19990827; NO 2001000957 A WO 1999-US19838 19990827, NO 2001-957 20010226; EP 1107974 A1 EP 1999-944004 19990827, WO 1999-US19838 19990827; US 6281381 B1 Provisional US 1998-98313P 19980827, Provisional US 1999-129743P 19990416, Provisional US 1999-144461P 19990719, US 1999-384145 19990827; CZ 2001000629 A3 WO 1999-US19838 19990827, CZ 2001-629 19990827; KR 2001079701 A KR 2001-702535 20010227; SK 2001000248 A3 WO 1999-US19838 19990827, SK 2001-248 19990827; BR 9913472 A BR 1999-13472 19990827, WO 1999-US19838 19990827; ZA 2001001451 A ZA 2001-1451 20010221; MX 2001002017 A1 MX 2001-2017 20010226; JP 2002523514 W WO 1999-US19838 19990827, JP 2000-567539 19990827; HU 2002003078 A2 WO 1999-US19838 19990827, HU 2002-3078 19990827; US 2003065214 A1 Cont of US 1999-384145 19990827, US 2001-898756 20010703; NZ 510682 A NZ 1999-510682 19990827, WO 1999-US19838 19990827; US 6696601 B2 Cont of US 1999-384145 19990827, US 2001-898756 20010703; US 2004158098 A1 Provisional US 1999-144461P 19990719, Cont of US 1999-384145 19990827, Cont of US

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US 2001-898756 20010703; US 2003-751237 20031231;
AU 2004-202301 20040526
IC ICM C07F000-00; C07F009-00; C07F009-28; C07F009-38
ICS A61K031-663; A61P019-08; A61P019-10
AB WO 200012517 A UPAB: 20021105
NOVELTY - 4-Amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt (I) with a water content of 1.3-11.7% is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the preparation of (I).
ACTIVITY - None given.
USE - Used for treating and/or preventing bone loss (claimed) including bone resorption in bone diseases such as in osteoporosis and Paget's disease.
ADVANTAGE - A 1-liter flask was fitted with a magnetic stirrer, Soxhlet extraction funnel (150 ml operating volume) charged with 3 Angstrom molecular sieves (60 g) and reflux condenser connected to a drying tube with 3 Angstrom molecular sieves. The flask was charged with **sodium alendronate trihydrate** (25 g) and absolute ethanol (450 ml, volume % of water less than 0.1%). The mixture was boiled with stirring for 24 hours. After cooling to ambient temperature, the solid material was filtered, washed with absolute ethyl ether and dried overnight in a vacuum oven (10-15 mmHg, ambient temperature) to give **sodium alendronate dihydrate.**
Dwg.0/8
FS CPI
FA AB; DCN
MC CPI: B05-B01G; B12-M11H; B14-N01

=> d all 140 tot

L40 ANSWER 1 OF 2 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1999-543525 [46] WPIX
CR 1999-142577 [12]; 2001-315983 [20]
DNC C2001-097572
TI Treatment of bone disorders with bisphosphonate on continuous dosage schedule, avoiding gastrointestinal side effects.
DC B05
IN DAIFOTIS, A G; SANTORA, A C; YATES, J A
PA (MERI) MERCK & CO INC
CYC 1
PI GB 2336311 A 19991020 (199946)* 48 A61K031-66
ADT GB 2336311 A GB 1998-19243 19980903
PRAI US 1998-134215 19980814; US 1998-60419 19980415;
US 1998-134214 19980814
IC ICM A61K031-66
AB GB 2336311 A UPAB: 20020213
NOVELTY - Treatment of Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, metastatic bone disease, hypercalcemia of malignancy and multiple myeloma comprises administration of a bisphosphonate (I) as a unit dosage on a continuous schedule one weekly, twice weekly, biweekly or twice monthly.
ACTIVITY - Osteopathic; antiinflammatory; cytostatic.

MECHANISM OF ACTION - Osteoclastic bone resorption inhibitor.
USE - (I) is useful for treatment of Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, metastatic bone disease, hypercalcemia of malignancy and multiple myeloma (claimed).
ADVANTAGE - The dosage regime of (I) allows effective dosing of (I) while lessening the gastrointestinal side effects (e.g. gastric esophageal reflux disease, esophagitis, dyspepsia, ulcers, esophageal irritation, esophageal perforation, abdominal pain or constipation) associated with a chronic dosage regime of (I) at low concentration on successive days. The more widely spaced dosage intervals increase patient compliance.
Dogs were dosed orally with 50 ml simulated gastric juice containing **alendronate monosodium trihydrate** (Ia) by direct infusion into the esophagus at 80 mg/ml once weekly for 4 weeks. 7 Days after the last dose, the animals were sacrificed and the esophagus removed and prepared for examination (embedded in paraffin and stained with hematoxylin and eosin). Histopathological studies showed an intact epithelium with no inflammation or vacuolation, compared with deep ulceration, marked submucosal inflammation and vacuolation in animals dosed with (Ia) once daily for 5 days and sacrificed immediately after the last dose.
Dwg.0/8

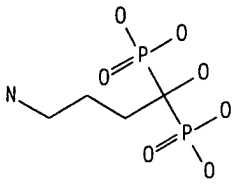
FS CPI
FA AB; DCN
MC CPI: B05-B01E; B05-B01F; B05-B01G; B06-D05; B07-A01; B07-D09; B07-F01; B14-H01; B14-L11; B14-N01; B14-N06

L40 ANSWER 2 OF 2 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN.S DCR-292621
DCSE 292621-0-1-0
CN.P SODIUM ALENDRONATE TRIHYDRATE
SY **ALENDRONATE MONOSODIUM TRIHYDRATE**; MONOSODIUM ALENDRONATE TRIHYDRATE; SODIUM ALENDRONATE TRIHYDRATE

CM 1

Na

CM 2



CMT A trihydrate of the above structure
MF Na . C4 H13 N O7 P2
SMF C4 H13 N O7 P2 *1; H2 O *3; Na *1; TOTAL *5; TYPE *3
MW 272.0881
SDCN RA1X5F

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L3            1 L1-2

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L8            1 L6-7

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FILE LAST UPDATED: 24 Feb 2005  (20050224/ED)

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 substance identification.


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L3   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2000:161293  HCAPLUS
DN   132:199040
ED   Entered STN:  10 Mar 2000
TI   Sodium alendronate hydrates, processes for their manufacture, and
     pharmaceutical compositions containing them
IN   Finkelstein, Nina; Lidor-Hadas, Ramy; Aronhime, Judith
PA   Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,
     Inc.
SO   PCT Int. Appl., 56 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   C07F009-38
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CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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	AU 9956988	A1	20000321	AU 1999-56988	19990827	<--
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	SI 20581	C	20011231	SI 1999-20070	19990827	<--
	BR 9913472	A	20020305	BR 1999-13472	19990827	<--
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	NO 2001000957	A	20010426	NO 2001-957	20010226	<--
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	US 6696601	B2	20040224			
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PRAI	US 1998-98313P	P	19980827			
	US 1999-129743P	P	19990416			
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	US 1999-384145	A1	19990827			
	WO 1999-US19838	W	19990827			
	US 2001-898756	A1	20010703			

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 2000012517	IC	C07F009-38	
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US 6281381	ECLA	C07F009/38A6U	<--
US 2003065214	ECLA	C07F009/38A6U	<--
US 2004158098	ECLA	C07F009/38A6U	<--

AB New hydrate forms of alendronate sodium, having water content of approx. 1-12%, and processes for their manufacture, are disclosed. New crystalline forms of alendronate sodium B, D, E, F, G and H, and processes for manufacturing them, are also disclosed. These new forms of alendronate sodium are suitable for incorporation into pharmaceutical compns. for combating bone resorption in bone diseases.

ST sodium alendronate hydrate prepn pharmaceutical; bone disease sodium alendronate hydrate prepn; resorption bone sodium alendronate hydrate prepn

IT Bone
(demineralization; sodium alendronate hydrates, preparation, and pharmaceutical compns.)

IT Ethers, miscellaneous
RL: MSC (Miscellaneous)
(polyalc.; sodium alendronate hydrates, preparation, and pharmaceutical compns.)

IT Alcohols, miscellaneous

RL: MSC (Miscellaneous)
(polyhydric, and polyalc. ethers; sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT Drug delivery systems
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT Alcohols, miscellaneous
RL: MSC (Miscellaneous)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT 138624-11-0P, Alendronic acid monohydrate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT 66376-36-1P, Alendronic acid
RL: PNU (Preparation, unclassified); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(reaction; sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT 124-41-4, Sodium methoxide 141-52-6, Sodium ethoxide 1310-73-2, Sodium hydroxide, reactions 7732-18-5, Water, reactions 121268-17-5 134606-40-9, Disodium alendronate 250665-54-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT 129318-43-0P, Monosodium alendronate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT 129318-43-0DP, Monosodium alendronate, hydrates 260055-00-3P 260055-01-4P 260055-02-5P 260055-03-6P 260055-04-7P 260055-05-8P 260055-06-9P 260055-07-0P 260055-08-1P 260055-09-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
IT 64-17-5, Ethanol, miscellaneous 67-56-1, Methanol, miscellaneous 67-63-0, 2-Propanol, miscellaneous 67-64-1, Acetone, miscellaneous 67-68-5, DMSO, miscellaneous 68-12-2, DMF, miscellaneous 75-05-8, Acetonitrile, miscellaneous 110-86-1, Pyridine, miscellaneous 123-91-1, Dioxane, miscellaneous 126-33-0, Sulfolane 872-50-4, miscellaneous
RL: MSC (Miscellaneous)
(sodium alendronate hydrates, preparation, and pharmaceutical compns.)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Blum; US 4624947 A 1986 HCAPLUS
(2) Brenner, G; WO 9639149 HCAPLUS
(3) Kieczykowski; US 4922007 A 1990 HCAPLUS
(4) Kieczykowski; US 5019651 A 1991 HCAPLUS
(5) Merck & Co Inc; WO 9639410 A1 1996 HCAPLUS
(6) Stahl; US 4639338 A 1987 HCAPLUS
(7) Stahl; US 4711800 A 1987

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FOR DETAILS. <<<

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L8 ANSWER 1 OF 1 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2000-246722 [21] WPIX
DNC C2000-074753
TI New 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt
with specified water content used to treat and/or prevent bone loss.
DC B05
IN ARONHIME, J; FINKELSTEIN, N; LIDOR-HADAS, R; LIDOR-HAMAS, R
PA (TEVA-N) TEVA PHARM IND LTD; (TEVA-N) TEVA PHARM USA INC; (ARON-I)
ARONHIME J; (FINK-I) FINKELSTEIN N; (LIDO-I) LIDOR-HADAS R
CYC 89
PI WO 2000012517 A1 20000309 (200021)* EN 56 C07F009-38
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US 2004158098 A1 20040812 (200454) C07F009-28 <--

AU 2004202301 A1 20040624 (200468)# C07F009-38

ADT WO 2000012517 A1 WO 1999-US19838 19990827; AU 9956988 A AU 1999-56988 19990827; NO 2001000957 A WO 1999-US19838 19990827, NO 2001-957 20010226; EP 1107974 A1 EP 1999-944004 19990827, WO 1999-US19838 19990827; US 6281381 B1 Provisional US 1998-98313P 19980827, Provisional US 1999-129743P 19990416, **Provisional US 1999-144461P 19990719**, US 1999-384145 19990827; CZ 2001000629 A3 WO 1999-US19838 19990827, CZ 2001-629 19990827; KR 2001079701 A KR 2001-702535 20010227; SK 2001000248 A3 WO 1999-US19838 19990827, SK 2001-248 19990827; BR 9913472 A BR 1999-13472 19990827, WO 1999-US19838 19990827; ZA 2001001451 A ZA 2001-1451 20010221; MX 2001002017 A1 MX 2001-2017 20010226; JP 2002523514 W WO 1999-US19838 19990827, JP 2000-567539 19990827; HU 2002003078 A2 WO 1999-US19838 19990827, HU 2002-3078 19990827; US 2003065214 A1 Cont of US 1999-384145 19990827, US 2001-898756 20010703; NZ 510682 A NZ 1999-510682 19990827, WO 1999-US19838 19990827; US 6696601 B2 Cont of US 1999-384145 19990827, US 2001-898756 20010703; US 2004158098 A1 **Provisional US 1999-144461P 19990719**, Cont of US 1999-384145 19990827, Cont of US 2001-898756 20010703, US 2003-751237 20031231; AU 2004202301 A1 Div ex AU 1999-56988 19990827, AU 2004-202301 20040526

FDT AU 9956988 A Based on WO 2000012517; EP 1107974 A1 Based on WO 2000012517; CZ 2001000629 A3 Based on WO 2000012517; SK 2001000248 A3 Based on WO 2000012517; BR 9913472 A Based on WO 2000012517; JP 2002523514 W Based on WO 2000012517; HU 2002003078 A2 Based on WO 2000012517; US 2003065214 A1 Cont of US 6281381; NZ 510682 A Based on WO 2000012517; US 6696601 B2 Cont of US 6281381; US 2004158098 A1 Cont of US 6281381, Cont of US 6696601

PRAI **US 1999-144461P 19990719**; US 1998-98313P 19980827; US 1999-129743P 19990416; US 1999-384145 19990827; US 2001-898756 20010703; US 2003-751237 20031231; AU 2004-202301 20040526

IC ICM C07F000-00; C07F009-00; C07F009-28; C07F009-38
ICS A61K031-663; A61P019-08; A61P019-10

AB WO 200012517 A UPAB: 20021105
NOVELTY - 4-Amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt (I) with a water content of 1.3-11.7% is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the preparation of (I).

ACTIVITY - None given.

USE - Used for treating and/or preventing bone loss (claimed) including bone resorption in bone diseases such as in osteoporosis and Paget's disease.

ADVANTAGE - A 1-liter flask was fitted with a magnetic stirrer, Soxhlet extraction funnel (150 ml operating volume) charged with 3 Angstrom molecular sieves (60 g) and reflux condenser connected to a drying tube with 3 Angstrom molecular sieves. The flask was charged with sodium alendronate trihydrate (25 g) and absolute ethanol (450 ml, volume % of water less than 0.1%). The mixture was boiled with stirring for 24 hours. After cooling to ambient temperature, the solid material was filtered, washed with absolute ethyl ether and dried overnight in a vacuum oven (10-15 mmHg, ambient temperature) to give sodium alendronate dihydrate.

Dwg.0/8

FS CPI

FA AB; DCN

MC CPI: B05-B01G; B12-M11H; B14-N01

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